ARTICLE 34 Amendment

CLAIMS

1. An antibody which is a modified version of a therapeutic antibody with affinity for a cell-surface antigen, said antibody having reduced affinity for the antigen compared with the therapeutic antibody as a result of a modification or modifications to the antibody molecule, wherein the antibody is capable of inducing immunological tolerance to the therapeutic antibody and wherein the antibody is not a mixed molecule antibody having an H or L chain of the therapeutic antibody paired with an L or H chain of an unrelated antibody.

2. An antibody as claimed in claim 1, wherein the framework regions of the variable domains of the antibody have the same or substantially the same amino acid sequence as the therapeutic antibody framework regions.

A 3. An antibody as claimed in claim 1 ~~or claim 2~~, wherein the modification comprises an alteration in at least one of the complementarity determining regions (CDRs).

4. An antibody as claimed in claim 3, wherein the alteration is achieved by genetic manipulation of a nucleic acid coding for the CDR.

A 5. An antibody as claimed in ~~any one of claims 1 to 4~~ Claim 1, wherein the affinity of the antibody for the antigen is reduced to 50% or less of the affinity of the therapeutic antibody.

A 6. An antibody as claimed in ~~any one of claims 1 to 5~~ Claim 1, wherein the CDRs are foreign with respect to the constant region of the antibody.

A 7. An antibody as claimed in ~~any one of claims 1 to 6~~ Claim 1, wherein the CDRs are foreign with respect to the heavy and light chain variable domain framework regions.

8. An antibody as claimed in claim 7, which is of substantially human origin other than the CDRs.

A 9. An antibody as claimed in ~~any one of claims 1 to 8~~ Claim 1, wherein

Amb D5

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Article 34 Amendment

Art 6 Cl

the therapeutic antibody has affinity for CD52.

10. An antibody as claimed in claim 9, wherein the therapeutic antibody is a humanised Campath-1 antibody

11. An antibody as claimed in claim 10, wherein the modification comprises an alteration in (VH) CDR2.

12. An antibody as claimed in claim 11, wherein the modification comprises a single or a double amino acid substitution in (VH) CDR2.

A Art 6 D7. 13. An antibody as claimed in ~~any one of claims 1 to 12~~ Claim 1, wherein the constant domains of the antibody have substantially the same amino acid sequence as the therapeutic antibody constant regions.

A Art 6 D8 A 14. A fragment of an antibody according to ~~any one of claims 1 to 13~~ Claim 1, which fragment retains tolerance-inducing capability of the antibody.

15. An antibody fragment as claimed in claim 14, which is a modified version of a therapeutic antibody fragment.

A Art 6 D9 A 16. An antibody or fragment as claimed in ~~any one of claims 1 to 15~~ Claim 1, which is monovalent.

A Art 6 D10 A 17. An antibody or fragment as claimed in ~~any one of claims 1 to 16~~ Claim 1, for inducing tolerance to the therapeutic antibody in a patient.

18. A cell line which expresses an antibody or fragment as claimed in ~~any one of claims 1 to 17~~ Claim 1.

Sub E1 A 19. A method of producing an antibody which is a modified version of a therapeutic antibody with affinity for a cell-surface antigen, said antibody having reduced affinity for the antigen compared with the therapeutic antibody as a result of a modification or modifications to the antibody molecule, wherein the antibody is capable of inducing immunological tolerance to the therapeutic antibody, comprising maintaining a cell line as claimed in claim 18 under conditions suitable for expression of said antibody or fragment thereof.

20. The method of claim 19, further comprising recovering the antibody or fragment.

Article 34 Amendment

21. The method of claim 20, further comprising isolating the antibody or fragment.

22 A composition for administration to a patient, comprising an antibody or fragment as claimed in any one of claims 1 to 17 or as produced by the method according to any one of claims 19 to 21, together with a physiologically acceptable diluent or carrier.

23. The use of an antibody or fragment as claimed in any one of claims 1 to 17 or as produced by the method according to any one of claims 19 to 21, in the manufacture of a medicament for the induction of tolerance.

sub A1

add A2

add E2

add D2

add D3